which the claims are directed. Applicants have amended the title to read: "Nucleic Acids Encoding Interleukin-1 Receptor Antagonist-Related-Proteins and Uses Thereof," which Applicants contend is clearly indicative of the invention to which the claims are directed.

2. Information Disclosure Statement

The Office Action states that Information Disclosure Statement filed March 26, 1997 fails to comply with the provisions of M.P.E.P. § 609 because an improper form PTO-1449 or equivalent was submitted. Specifically, the Action states that each of the EMBL database submissions listed on the IDS fails to recite the name of the author and the date of publication. The Action also notes that the names of the authors and the date of publications for these EMBL database submissions have been added to the form PTO-1449, with the corrected document being made of record.

Applicants presume that the Information Disclosure Statement of which the Action refers is the Information Disclosure Statement filed June 21, 2001. Applicants thank the Examiner for correcting the form PTO-1449 by adding the names of the authors and the date of publications for the EMBL database submissions. Applicants believe that the corrected form PTO-1449 complies with the provisions of M.P.E.P. § 609, and note that the Action states that the corrected PTO-1449 has been made of record. However, Applicants would be happy to supply an updated copy of the Information Disclosure Statement, and would prefer to have the opportunity if the deficiencies in their previously-submitted Information Disclosure Statement will have the effect of leaving any of the cited references off the front page of any issued patent.

3. Rejections of claims 1-8, 10, 11, and 42-46 under 35 U.S.C. § 112, first paragraph

The Office Action asserts a rejection of claims 1, 2, 4-8, 10, 11, and 42-46, under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention. The Action states that a deposit of biological material is necessary for the enablement of the claims because the specification does not provide a repeatable method for obtaining ATCC Deposit No. PTA-1423 and this deposit does not appear to be a readily available material. The Action also states that a deposit made in full compliance with 37 C.F.R. §§ 1.803-1.809 would satisfy the requirements of 35 U.S.C. § 112, first paragraph, provided that Applicants

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submit an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that a deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent.

Pursuant to the Examiner's request, Applicants submit herewith a Declaration stating that a deposit complying with 37 C.F.R. §§ 1.801-1.809 was made under the provisions of the Budapest Treaty. Applicants contend that all the requirements of 37 C.F.R. §§ 1.801-1.809 have been met. *In re Lundak*, 225 U.S.P.Q. 90 (Fed. Cir. 1985). Withdrawal of this rejection is therefore respectfully solicited.

The Office Action also asserts a rejection of claims 2, 3-8, 10, 11, and 42-46, under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Action states that because the genus of IL-1ra-R variants recited in claims 2 and 3 is highly variant, and the specification fails to describe the common attributes or characteristics identifying the members of this genus, or provide a representative number of species to describe this genus, the Applicants were not in possession of the claimed genus of nucleic acid molecules at the time the application was filed.

Applicants have amended claim 2 to recite an isolated nucleic acid molecule comprising a region of the nucleotide sequence of SEQ ID NO: 1, or the DNA insert in ATCC Deposit No. PTA-1423, encoding a polypeptide fragment of at least 25 amino acid residues, wherein the polypeptide fragment has an activity of the polypeptide set forth in SEQ ID NO: 2, or is antigenic; a region of the nucleotide sequence of SEQ ID NO: 1, or the DNA insert in ATCC Deposit No. PTA-1423, comprising a fragment of at least 16 nucleotides; a nucleotide sequence that hybridizes under at least moderately stringent conditions to the complement of the nucleotide sequence of either of these nucleic acid molecules; or a nucleotide sequence complementary to the nucleotide sequence of any of the above nucleic acid molecules. Applicants contend that because claim 2, as amended, recites only fragments of the disclosed human IL-1ra-R nucleic acid molecule (*i.e.*, SEQ ID NO: 1), one of ordinary skill in the art could readily determine the structure of nucleic acid molecules falling within the scope of this claim. Applicants therefore respectfully request that this ground of rejection be

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withdrawn.

Applicants have amended claim 3 to recite an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one conservative amino acid substitution, wherein the encoded polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 2; a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 having a C- and/or N- terminal truncation, wherein the encoded polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 2; a region of the nucleotide sequence of any of these nucleic acid molecules comprising a fragment of at least 16 nucleotides; a nucleotide sequence that hybridizes under at least moderately stringent conditions to the complement of the nucleotide sequence of any of the above nucleic acid molecules; or a nucleotide sequence complementary to any of the above nucleic acid molecules. Applicants note that the instant application teaches the amino acid sequences for human and murine IL-1ra-R polypeptide (Figures 1A-1B and Figure 7). The instant application also teaches that conservative amino acid substitutions may be made in those portions of the IL-1ra-R polypeptide that are not identical among IL-1ra-R orthologs (page 28, lines 4-14). The instant application further sets forth in Table I (pages 27-28) rubrics recognized in the art for making conservative amino acid substitutions. Finally, the specification discloses a sequence comparison so illustrating conserved amino acid residues in the IL-1ra-R polypeptide sequence (Figure 8). In view of the teachings in the instant application, Applicants respectfully contend that one of ordinary skill in the art would understand the scope of species comprising the disclosed genus, and that the inventors were in possession of the invention having said scope at the time the application was filed. Thus, Applicants respectfully contend that their specification fulfills the requirements of 35 U.S.C. § 112, first paragraph, and request that this ground of rejection be withdrawn.

The Office Action also asserts a rejection of claims 2-8, 10, 11, and 42-46, under 35 U.S.C. § 112, first paragraph, because the specification while being enabling for a nucleic acid encoding a polypeptide as set forth in SEQ ID NO: 2, does not reasonably provide enablement for a nucleic acid encoding a polypeptide which is "at least about 70% identical to the polypeptide of SEQ ID NO: 2" or a nucleic acid molecule encoding a substitution, insertion, or deletion mutant of the polypeptide of SEQ ID NO: 2. The Action states that because the claims are overly broad, no guidance is provided in the specification as to how one of ordinary skill in the art would generate a nucleic acid molecule encoding an IL-1ra-R polypeptide other than the one exemplified in the specification, and it is known

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in the art that even a single amino acid change in the amino acid sequence of a protein can have a dramatic effect on that protein's function, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

As described above, Applicants have amended claims 2 and 3 so that they no longer recite nucleic acid molecules comprising either a nucleotide sequence encoding a polypeptide which is at least about 70 percent identical to the polypeptide as set forth in any of SEQ ID NO: 2; a nucleotide sequence encoding an allelic variant or splice variant of the nucleotide sequence as set forth in any of SEQ ID NO: 1; a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one amino acid insertion; or a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one amino acid deletion. Applicants contend that the claims, as amended, are not overly broad, and that in view of the specification's teachings, one of ordinary skill in the art could readily make and use the claimed nucleic acid molecules. Moreover, Applicants contend that while the references cited in the Action may teach that an amino acid change in the amino acid sequence of a protein can have a dramatic effect on that protein's function, these references do *not* teach that a *conservative* amino acid substitution would have this effect. Specifically, Mikayama *et al.*, 1993, *Proc. Natl. Acad. Sci.* U.S.A. 90:10056-60, teach that an asparagine-to-serine substitution at position 106 in human GIF destroys GIF function, and Voet *et al.*, *Biochemistry* 126-28, 228-34 (1990), teach that a glutamic acid-to-valine substitution in beta hemoglobin results in sickle-cell anemia. These are *not* "conservative substitutions" as that term is understood by those with skill in the art *or* as explicitly defined in the instant specification. Applicants note that the instant specification does not teach that an asparagines-to-serine substitution or a glutamic acid-to-valine substitution is either exemplary or preferred (Table 1; pages 29-30). Applicants contend that, in view of the specification's teachings and knowledge in the art, it would not require undue experimentation for one of ordinary skill in the art to make and use the claimed invention, and therefore, Applicants respectfully request that this ground of rejection be withdrawn.

Applicants respectfully contend that rejections based on 35 U.S.C. § 112, first paragraph, have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

4. Rejections of claims 1-8, 10, 11, and 42-46 under 35 U.S.C. § 112, second paragraph

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The Office Action asserts a rejection of claims 1-8, 10, 11, and 42-46, under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as their invention.

The Action first asserts that claims 1-3 are indefinite for reciting the phrase "hybridizes under moderately or highly stringent conditions" because this phrase is relative and conditional. The Action states that some nucleic acids which might hybridize under conditions of moderate stringency would fail to hybridize under conditions of high stringency. Applicants note that the specification defines the meaning of the terms "moderately stringent conditions" (page 23, lines 17-24) and "highly stringent conditions" (page 22, lines 12-19), and provides examples of each. However, in order to more particularly point out and distinctly claim the subject matter that Applicants regard as their invention, Applicants have amended claims 1-3 to recite that the claimed nucleic acid molecules comprise a nucleotide sequence that "hybridizes under at least moderately stringent conditions." Applicants contend that the claims, as amended, are not indefinite, and therefore, respectfully request that this ground of rejection be withdrawn.

The Action next asserts that claim 2 is vague for reciting the phrase "about 70% identical" because the term "about" is inherently vague and indefinite. The Action states that the use of the term "about" is appropriate when defining an invention in terms of indefinitely divisible units, such as inches or meters, but not when defining an invention in terms of indivisible numerical units, such as the percent identity in the number of amino acids in a polypeptide. As discussed in section 3 above, Applicants have amended claim 2 so that it no longer recites a nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide which is at least about 70 percent identical to the polypeptide as set forth in any of SEQ ID NO: 2. In addition, Applicants have amended claim 2 to replace the term "about 25 amino acid residues" with the term "25 amino acid residues," and claims 2 and 3 to replace the term "about 16 nucleotides" with the term "16 nucleotides." Applicants contend that the claims, as amended, are not indefinite, and therefore, respectfully request that this ground of rejection be withdrawn.

The Action next asserts that claims 2 and 3 are vague and indefinite for reciting the phrase "has an activity of the polypeptide set forth in...SEQ ID NO: 2" because the activity of the polypeptide encoded by the nucleic acid being claimed is unclear. Applicants contend, however, that claims containing this limitation encompass only those nucleic acid molecules encoding IL-1ra-R

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polypeptide variants that possess an inherent activity of the polypeptide as set forth in SEQ ID NO: 2. Applicants teach the expression of human IL-1ra-R mRNA in adult gall bladder, peripheral blood leukocytes, and placenta, and in fetal scalp, eye, and spleen (page 110, lines 23-26; page 111, lines 11-12). The expression of IL-1ra-R polypeptides in these tissues indicates that IL-1ra-R polypeptide has an inherent function that will be possessed by any species falling within the scope of the amended claim. In view of the inherency of activity that resides in polypeptides having the amino acid sequence as set forth in SEQ ID NO. 2, Applicants contend that the term is not indefinite, and therefore, respectfully request that this ground of rejection be withdrawn.

The Action next asserts that claim 10 is vague and indefinite for reciting the phrase "other than the promoter DNA for the native IL-1ra-R polypeptide" because it is unclear which promoter DNA is being excluded and which is being included in the claim. Applicants have amended claim 10 to recite that "the nucleic acid molecule comprises promoter DNA other than native IL-1ra-R promoter DNA." Applicants contend that because it is clear which promoter DNA is being excluded and which is being included, claim 10 is not indefinite, and therefore, respectfully request that this ground of rejection be withdrawn.

The Action next asserts that claim 46 is indefinite for reciting the term "fragment[s] thereof" because this term encompasses potentially any portion of the heterologous polypeptide including a single amino acid. Applicants have amended claim 46 to recite that the IgG constant domain fragment must be "biologically-active," and therefore, respectfully request that this ground of rejection be withdrawn.

The Action next asserts that claims 45 and 46, which are dependent upon non-elected claims 13, 14, 15, 55, or 56, should be amended to be dependent upon on elected nucleic acid claims, since the nucleic acid is utilized in production of the fusion proteins. Applicants have amended claims 45 and 46 to recite a nucleic acid molecule encoding a fusion polypeptide comprising the nucleic acid molecule of any of claims 1, 2, or 3 fused to DNA encoding a heterologous amino acid sequence. Because claims 45 and 46, as amended, are no longer dependent upon non-elected claims 13, 14, 15, 55, or 56, Applicants request that this ground of rejection be withdrawn.

The Action next asserts that claims 1-3 are improper for reciting non-elected sequences. Applicants have amended the claims so that they no longer recite non-elected sequences, and therefore, respectfully request that this ground of rejection be withdrawn.

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The Action next asserts that claims 4-8, 11, and 42-44 are vague and indefinite for being dependent upon claims 1 and 2 for their limitations. Applicants contend that the claims, as amended, satisfy the requirements of 35 U.S.C. § 112, second paragraph, and therefore, respectfully contend that this ground of rejection be withdrawn.

Applicants respectfully contend that rejections based on 35 U.S.C. § 112, second paragraph, have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

5. Rejections of claims 1-8, 10, 11, and 42-46 under 35 U.S.C. § 102

The Office Action asserts a rejection of claims 1-8, 10, 11, and 42-46, under 35 U.S.C. § 102(a), as being anticipated by International Publication No. WO 99/37662 (published July 29, 1999), contending that this reference discloses a nucleotide sequence of a cDNA molecule encoding a SPOIL protein, which would be capable of hybridizing under moderately stringent conditions to the complement of the nucleotide sequence of SEQ ID NO: 1, or which, in the absence of an upper limit to the number of substitutions, deletions, or insertions, would meet the limitations of claim 3. Applicants traverse this rejection.

Applicants first note that the cDNA molecule disclosed in International Publication No. WO 99/37662 shares a sequence identity of only 32.4% with the nucleotide sequence of SEQ ID NO: 1 (Exhibit A). In view of the specification's teaching that nucleic acid molecules capable of hybridizing under moderately stringent conditions will share a sequence identity of approximately 79% (page 23, lines 23-24), it is quite apparent that the cDNA molecule disclosed in WO 99/37662 would *not* hybridize to the nucleotide sequence of SEQ ID NO: 1 under Applicants' recited stringency conditions. Moreover, Applicants contend that because the cDNA molecule disclosed in WO 99/37662 shares little sequence identity with the nucleotide sequence of SEQ ID NO: 1, the protein encoded by that cDNA molecule will *not* possess an inherent activity of the IL-1ra-R polypeptide set forth in SEQ ID NO: 2, as required by claims 2 and 3. Applicants contend, therefore, that International Publication No. WO 99/37662 cannot anticipate the claims of the instant application, and respectfully request that this ground of rejection be withdrawn.

The Office Action next asserts a rejection of claims 1-8, 10, 11, and 42-46, under 35 U.S.C. § 102(b), as being anticipated by European Patent Application No. EP 0 855 404 (published July 29,

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1998), contending that this reference discloses a nucleotide sequence of a cDNA molecule encoding an IL-1ra beta protein, which would be capable of hybridizing under moderately stringent conditions to the complement of the nucleotide sequence of SEQ ID NO: 1, or which, in the absence of an upper limit to the number of substitutions, deletions, or insertions, would meet the limitations of claim 3. Applicants traverse this rejection.

Applicants first note that the cDNA molecule disclosed in European Patent Application No. EP 0 855 404 shares a sequence identity of only 50.9% with the nucleotide sequence of SEQ ID NO: 1 (Exhibit B). As discussed above, in view of the specification's teaching that nucleic acid molecules capable of hybridizing under moderately stringent conditions will share a sequence identity of approximately 79%, it is quite apparent that the cDNA molecule disclosed in EP 0 855 404 would *not* hybridize to the nucleotide sequence of SEQ ID NO: 1 under Applicants' recited stringency conditions. Moreover, Applicants contend that because the cDNA molecule disclosed in EP 0 855 404 shares little sequence identity with the nucleotide sequence of SEQ ID NO: 1, the protein encoded by that cDNA molecule will *not* possess an inherent activity of the IL-1ra-R polypeptide set forth in SEQ ID NO: 2, as required by claims 2 and 3. Applicants contend, therefore, that European Patent Application No. EP 0 855 404 cannot anticipate the claims of the instant application, and respectfully request that this ground of rejection be withdrawn.

The Office Action next asserts a rejection of claims 1-8, 10, and 42, under 35 U.S.C. § 102(b), as being anticipated by U.S. Patent No. 5,075,222 (issued December 24, 1991), contending that this reference discloses a nucleotide sequence of a cDNA molecule encoding an IL-1ra protein, which would be capable of hybridizing under moderately stringent conditions to the complement of the nucleotide sequence of SEQ ID NO: 1, or which, in the absence of an upper limit to the number of substitutions, deletions, or insertions, would meet the limitations of claim 3. Applicants traverse this rejection.

Applicants first note that the cDNA molecule disclosed in U.S. Patent No. 5,075,222 shares a sequence identity of only 28.8% with the nucleotide sequence of SEQ ID NO: 1 (Exhibit C). As discussed above, in view of the specification's teaching that nucleic acid molecules capable of hybridizing under moderately stringent conditions will share a sequence identity of approximately 79%, it is quite apparent that the cDNA molecule disclosed in U.S. 5,075,222 would *not* hybridize to the nucleotide sequence of SEQ ID NO: 1 under Applicants' recited stringency conditions.

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Moreover, Applicants contend that because the cDNA molecule disclosed in U.S. 5,075,222 shares little sequence identity with the nucleotide sequence of SEQ ID NO: 1, the protein encoded by that cDNA molecule will *not* possess an inherent activity of the IL-1ra-R polypeptide set forth in SEQ ID NO: 2, as required by claims 2 and 3. Applicants contend, therefore, that U.S. Patent No. 5,075,222 cannot anticipate the claims of the instant application, and respectfully request that this ground of rejection be withdrawn.

Applicants respectfully contend that rejections based on 35 U.S.C. § 102 have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

CONCLUSIONS

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended. Allowance of the claims is thereby respectfully solicited.

If Examiner Mertz believes it to be helpful, she is invited to contact the undersigned representative by telephone at (312) 913-0001.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff

Dated: January 2, 2003

By: Donald L. Zuhn, Ph.D.
Reg. No. 48,710

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AMENDMENTS TO THE SPECIFICATION

Marked Up Version of Replacement Paragraphs of Specification

under 37 C.F.R. 1.121(b)(1)(iii)

Please amend the title at page 2, lines 1-2 to read as follows:

NUCLEIC ACIDS ENCODING INTERLEUKIN-1 RECEPTOR ANTAGONIST-RELATED ~~MOLECULES~~ PROTEINS AND USES THEREOF

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AMENDMENTS TO THE CLAIMS

Marked Up Versions of Amended Claims under 37 C.F.R. 1.121(c)(1)(ii)

1. (Amended) An isolated nucleic acid molecule comprising a nucleotide sequence ~~selected from the group consisting of~~:

(a) ~~the nucleotide sequence~~ as set forth in ~~any of~~ SEQ ID NO: 1~~, SEQ ID NO: 3, SEQ ID NO: 5, or SEQ ID NO: 35~~;

(b) ~~the nucleotide sequence~~ of the DNA insert in ATCC Deposit No. PTA-1423;

(c) ~~a nucleotide sequence~~ encoding ~~the~~ a polypeptide as set forth in ~~any of~~ SEQ ID NO: 2~~, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36~~;

(d) ~~a nucleotide sequence which~~that hybridizes under at least moderately ~~or highly~~ stringent conditions to the complement of the nucleotide sequence of any of (a) - (c), ~~and~~ or

(e) ~~a nucleotide sequence~~ complementary to the nucleotide sequence of any of (a) - ~~(e)~~(d).

2. (Amended) An isolated nucleic acid molecule comprising ~~a nucleotide sequence selected from the group consisting of~~:

~~(a) a nucleotide sequence encoding a polypeptide which is at least about 70 percent identical to the polypeptide as set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36, wherein the encoded polypeptide has an activity of the polypeptide set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36;~~

~~(b) a nucleotide sequence encoding an allelic variant or splice variant of the nucleotide sequence as set forth in any of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, or SEQ ID NO: 35, the nucleotide sequence of the DNA insert in ATCC Deposit No. PTA-1423, or (a);~~

~~(c)~~(a) a region of the nucleotide sequence of ~~any of~~ SEQ ID NO: 1~~, SEQ ID NO: 3, SEQ ID NO: 5, or SEQ ID NO: 35~~, or the DNA insert in ATCC Deposit No. PTA-1423, ~~(a), or (b)~~ encoding a polypeptide fragment of at least ~~about~~ 25 amino acid residues, wherein the polypeptide fragment has an activity of the ~~encoded~~ polypeptide ~~as~~ set forth in ~~any of~~ SEQ ID NO: 2~~, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36~~, or is antigenic;

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~~(d)~~(b) a region of the nucleotide sequence of ~~any of~~ SEQ ID NO: 1~~, SEQ ID NO: 3, SEQ ID NO: 5, or SEQ ID NO: 35~~, or the DNA insert in ATCC Deposit No. PTA-1423, ~~or any of (a) - (c)~~ comprising a fragment of at least ~~about~~ 16 nucleotides;

~~(e)~~(c) a nucleotide sequence ~~which~~ that hybridizes under at least moderately ~~or highly~~ stringent conditions to the complement of the nucleotide sequence of either ~~any of~~ (a) ~~- (d)~~ or (b); ~~and~~ or

~~(f)~~(d) a nucleotide sequence complementary to the nucleotide sequence of any of (a) - ~~(d)~~(c).

3. (Amended) An isolated nucleic acid molecule comprising ~~a nucleotide sequence selected from the group consisting of~~:

(a) a nucleotide sequence encoding a polypeptide as set forth in ~~any of~~ SEQ ID NO: 2~~, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36~~ with at least one conservative amino acid substitution, wherein the encoded polypeptide has an activity of the polypeptide set forth in ~~any of~~ SEQ ID NO: 2~~, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36~~;

~~(b) a nucleotide sequence encoding a polypeptide as set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36 with at least one amino acid insertion, wherein the encoded polypeptide has an activity of the polypeptide set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36;~~

~~(c) a nucleotide sequence encoding a polypeptide as set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36 with at least one amino acid deletion, wherein the encoded polypeptide has an activity of the polypeptide set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36;~~

~~(d)~~(b) a nucleotide sequence encoding a polypeptide as set forth in ~~any of~~ SEQ ID NO: 2~~, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36 which~~ ~~has~~ving a C- and/or N- terminal truncation, wherein the encoded polypeptide has an activity of the polypeptide set forth in ~~any of~~ SEQ ID NO: 2~~, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36~~;

~~(e)~~(c) a nucleotide sequence encoding a polypeptide as set forth in ~~any of~~ SEQ ID NO: 2~~, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36~~ with at least one modification ~~selected from the group consisting of~~ that is a conservative amino acid substitutions~~, amino acid insertions,~~

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~~amino acid deletions;~~ C-terminal truncation, ~~and~~ or N-terminal truncation, wherein the encoded polypeptide has an activity of the polypeptide set forth in ~~any of~~ SEQ ID NO: 2~~, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36~~;

~~(f)~~(d) a region of the nucleotide sequence of any of (a) - ~~(e)~~(c) comprising a fragment of at least ~~about~~ 16 nucleotides;

~~(g)~~(e) a nucleotide sequence ~~which~~that hybridizes under at least moderately ~~or highly~~ stringent conditions to the complement of the nucleotide sequence of any of (a) - ~~(f)~~(d)~~, and~~ or

~~(h)~~(f) a nucleotide sequence complementary to any of (a) - (e).

10. (Amended) The process of Claim 8, wherein the nucleic acid molecule comprises promoter DNA other than ~~the promoter DNA for the~~ native IL-1ra ~~R polypeptide~~ promoter DNA operatively linked to ~~the DNA~~ a nucleic acid molecule encoding ~~the~~ an IL-1ra R polypeptide.

11. (Amended) The isolated nucleic acid molecule according to Claim 2, wherein the percent identity is determined using a computer program ~~selected from the group consisting of~~ that is GAP, BLASTN, FASTA, BLASTA, BLASTX, BestFit, ~~and~~ or the Smith-Waterman algorithm.

45. (Amended) A nucleic acid molecule encoding a fusion polypeptide comprising the ~~polypeptide~~ nucleic acid molecule of any of Claims ~~13, 14, 15, 55, or 56~~ 1, 2, or 3 fused to DNA encoding a heterologous amino acid sequence.

46. (Amended) The ~~fusion polypeptide~~ nucleic acid molecule of Claim 45, wherein the DNA encoding the heterologous amino acid sequence ~~is~~ encodes an IgG constant domain or biologically active fragment thereof.

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EXHIBIT A

```
                10        20        30        40        50
SEQ02_nuc       CAGGGATCAGGGTTCCAGGAACTCAGGATCTGCAGTGAGGACCAGACACC
                GTCCCTAGTCCCAAGGTCCTTGAGTCCTAGACGTCACTCCTGGTCTGTGG

                60        70        80        90        100
SEQ02_nuc       ACTGATTGCAGGAATGTGTTCCCTCCCCATGGCAAGATACTACATAATTA
                TGACTAACGTCCTTACACAAGGGAGGGGTACCGTTCTATGATGTATTAAT

                110       120       130       140       150
SEQ02_nuc       AATATGCAGACCAGAAGGCTCTATACACAAGAGATGGCCAGCTGCTGGTG
                TTATACGTCTGGTCTTCCGAGATATGTGTTCTCTACCGGTCGACGACCAC

                160       170       180       190       200
SEQ02_nuc       GGAGATCCTGTTGCAGACAACTGCTGTGCAGAGAAGATCTGCACACTTCC
                CCTCTAGGACAACGTCTGTTGACGACACGTCTCTTCTAGACGTGTGAAGG

                210       220       230       240       250
SEQ02_nuc       TAACAGAGGCTTGGACCGCACCAAGGTCCCCATTTTCCTGGGGATCCAGG
                ATTGTCTCCGAACCTGGCGTGGTTCCAGGGGTAAAAGGACCCCTAGGTCC

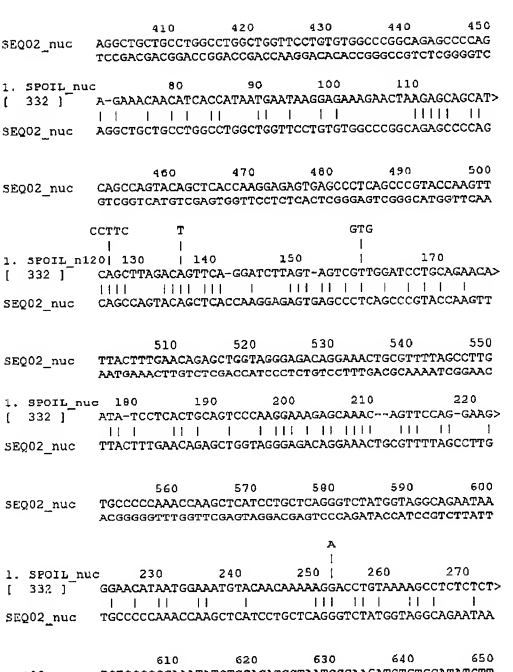
                260       270       280       290       300
SEQ02_nuc       GAGGGAGCCGCTGCCTGGCATGTGTGGAGACAGAAGAGGGGCCTTCCCTA
                CTCCCTCGGCGACGGACCGTACACACCTCTGTCTTCTCCCCGGAAGGGAT

                310       320       330       340       350
SEQ02_nuc       CAGCTGGAGGATGTGAACATTGAGGAACTGTACAAAGGTGGTGAAGAGGC
                GTCGACCTCCTACACTTGTAACTCCTTGACATGTTTCCACCACTTCTCCG

1. SPOIL_nuc                                  10        20
[  332 ]                                      CGGCACGAGGGTAGTG-TGCAGA>
                                              | | || | ||| ||| |  |
SEQ02_nuc                                     CTGTACAAAGGTGGTGAAGAGGC

                360       370       380       390       400
SEQ02_nuc       CACACGCTTCACCTTCTTCCAGAGCAGCTCAGGCTCCGCCTTCAGGCTTG
                GTGTGCGAAGTGGAAGAAGGTCTCGTCGAGTCCGAGGGCGGAAGTCCGAAC

1. SPOIL_nuc 30        40        50        60        70
[  332 ]     CACA---TTCCTATTCAATCAG-G--G-TCAATCTGCAGATTGGCAGCTC>
             ||||   |||   |||   ||| |  | |||  || |   ||     |
SEQ02_nuc    CACACGCTTCACCTTCTTCCAGAGCAGCTCAGGCTCCGCCTTCAGGCTTG
```



```
                660        670        680        690        700
SEQ02_nuc   ACCATACATGTCCAAAGAGGTTTTGCAAATGTGATTATGTTAAGGATCTT
            TGGTATGTACAGGTTTCTCCAAAACGTTTACACTAATACAATTCCTAGAA

                                  C
                                  |
1. SPOIL_nuc      330        340 |  350        360        370
[  332 ]    CCCTGGTTGGTTCATCGCTGTTGCTCTAAAGGGAGCTGCCCACTCATTCT>
             ||     || ||   |  |||    | || | ||          |   ||  |
SEQ02_nuc   ACCATACATGTCCAAAGAGGTTTTGCAAATGTGATTATGTTAAGGATCTT

                710        720        730        740        750
SEQ02_nuc   GAAATGAGGAGACAATCCTGGGTTATCCTTGTGGGCTCAGTTTAATCACA
            CTTTACTCCTCTGTTAGGACCCAATAGGAACACCCGAGTCAAATTAGTGT

          CCCAAG
            |
1. SPOIL_nuc |      390        400        410        420
[  332 ]    GAAACTGGGGGA-AATCTTCATCACTGACTTCGAGATGATTGTGGT-ACA>
            ||||   || || |||| !        |   | | | | | | |  | |||
SEQ02_nuc   GAAATGAGGAGACAATCCTGGGTTATCCTTGTGGGCTCAGTTTAATCACA

                760        770        780        790        800
SEQ02_nuc   AGAAGGAGGCAGGAAGGGAGAGTCAGAGAGAGAATGGAAGATACCATGCT
            TCTTCCTCCGTCCTTCCCTCTCAGTCTCTCTCTTACCTTCTATGGTACGA

                                                C          C
                                                |          |
1. SPOIL_nuc430        440        450        460 |  470     |
[  332 ]    TTAAGGTTTTTAGACACATTGCTCTGTGGCACTCTTCAAGATTTCTTGAT>
              ||||       ||          || | |  |   |  |  |||||  | || |
SEQ02_nuc   AGAAGGAGGCAGGAAGGGAGAGTCAGAGAGAGAATGGAAGATACCATGCT

                810        820        830        840        850
SEQ02_nuc   TCTAATTTTGAAGATGGAGTGAGGGGCCTTGAGCCAACAAATGCAGGTGT
            AGATTAAAACTTCTACCTCACTCCCCGGAACTCGGTTGTTTACGTCCACA

                      C
                      |
1. SPOIL_n480        490|     500        510          520
[  332 ]    TCTAA-CAAGAAGAATCAAAGA-CACCCCTAA--CA--AAATGGAAGACT>
            |||||   |||||   |  ||    || | |  ||  ||||| | |  |
SEQ02_nuc   TCTAATTTTGAAGATGGAGTGAGGGGCCTTGAGCCAACAAATGCAGGTGT

                860        870        880        890        900
SEQ02_nuc   TTTTAGAAGGTGGAAAAGCCAAGGGAACGGATTCTCCTCTAGAGTCTCCG
            AAAATCTTCCACCTTTTCGGTTCCCTTGCCTAAGAGGAGATCTCAGAGGC

1. SPOIL_nuc  530        540        550        560        570
[  332 ]    GAAAAGAAAGCTGAGCCCTCCCTGG-GCTGTTTTTCCTTGGTGGTGAATC>
              |||| |  ||     |  ||  | | || ||||      ||
SEQ02_nuc   TTTTAGAAGGTGGAAAAGCCAAGGGAACGGATTCTCCTCTAGAGTCTCCG
```

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                910        920        930        940        950
SEQ02_nuc   GAAGGAACACAGCTCTTGACACATGGATTTCAGCTCAGTGACACCCATTT
            CTTCCTTGTGTCGAGAACTGTGTACCTAAAGTCGAGTCACTGTGGGTAAA

1. SPOIL_nuc    580        590        600                610
[  332 ]    AGATGAAGA-ACATCTT-AC-CAT-GTTTTCATC-CA---A-A-GCATTT>
              | ||| | |  |||| || ||| | ||||| | ||   | |  |||||
SEQ02_nuc   GAAGGAACACAGCTCTTGACACATGGATTTCAGCTCAGTGACACCCATTT

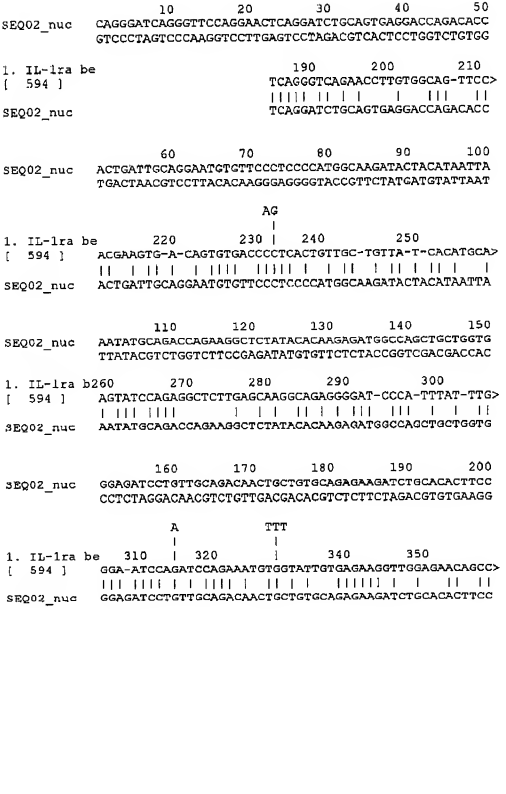

                960        970        980        990       1000
SEQ02_nuc   CAGACTTCTGACCTCCACAACTATAAAATAATAAACTTGTGTTATTGTAA
            GTCTGAAGACTGGAGGTGTTGATATTTATTATTTGAACACAATAACATT

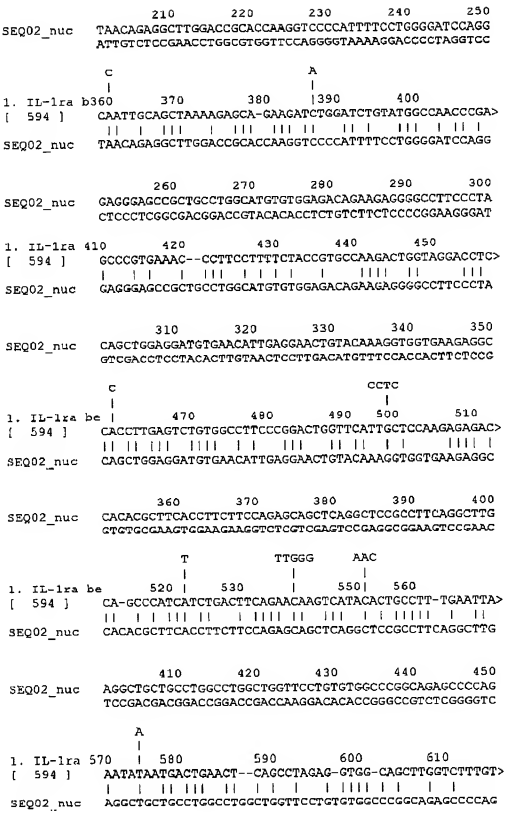
                                  GT
                                   |
1. SPOIL_nuc        620        630  |  640        650          660
[  332 ]    ---ACTGTTGGTTTTTACAAGGAGAATTTTTTAAAATAAAATCATT-T-A>
               |||  ||    |  ||||  | ||  |  |||| |     | ||| | |
SEQ02_nuc   CAGACTTCTGACCTCCACAACTATAAAATAATAAACTTGTGTTATTGTAA


               1010       1020
SEQ02_nuc   ACCTCTAAAAAAAAAAAAAA
            TGGAGATTTTTTTTTTTTTT

1. SPOIL_nuc        670        680
[  332 ]    TCTCATAAAAAAAAAAAAAA>
             |   ||||||||||||||
SEQ02_nuc   ACCTCTAAAAAAAAAAAAAA
```

EXHIBIT B





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                460       470       480       490       500
SEQ02_nuc   CAGCCAGTACAGCTCACCAAGGAGAGTGAGCCCTCAGCCCGTACCAAGTT
            GTCGGTCATGTCGAGTGGTTCCTCTCACTCGGGAGTCGGGCATGGTTCAA

                    T
                    |
1. IL-1ra be 620    |  630       640       650       660
[  594 ]    CTTAAAGTTCTGGTTCCCAATGTGTTTTCG-TCT-A-CATTTTCTTAGTG>
            |    ||| | | |  |||| | |   |   |  || | |   | |  |||
SEQ02_nuc   CAGCCAGTACAGCTCACCAAGGAGAGTGAGCCCTCAGCCCGTACCAAGTT

                510       520       530       540       550
SEQ02_nuc   TTACTTTGAACAGAGCTGGTAGGGAGACAGGAAACTGCGTTTTAGCCTTG
            AATGAAACTTGTCTCGACCATCCCTCTGTCCTTTGACGCAAAATCGGAAC

                                        GGG  G    T ATC
                                         |   |    |  |
1. IL-1ra be    670           680        |   |700 | 710
[  594 ]    TCA-TTT--TCA-CGCTGGTGCTGAGACAGGAAGCTGCGTTATCTCATTT>
            | | |||   ||  ||||||   |||||||  || |||||||  |  | ||
SEQ02_nuc   TTACTTTGAACAGAGCTGGTAGGGAGACAGGAAACTGCGTTTTAGCCTTG

                560       570       580       590       600
SEQ02_nuc   TGCCCCCAAACCAAGCTCATCCTGCTCAGGGTCTATGGTAGGCAGAATAA
            ACGGGGGTTTGGTTCGAGTAGGACGAGTCCCAGATACCATCCGTCTTATT

                    G
                    |
1. IL-1ra b720      730       740       750       760
[  594 ]    TATAATGAAAAGAAGCAATTAGTTCATAGCAACTGAAG-A-ACAGCAT-C>
            |     |||  ||||   | || |  ||   ||   | |  ||| ||
SEQ02_nuc   TGCCCCCAAACCAAGCTCATCCTGCTCAGGGTCTATGGTAGGCAGAATAA

                610       620       630       640       650
SEQ02_nuc   TGTCCCCCGAAATATGTCCACATCCTAATCCCAAGATCTGTGCATATGTT
            ACAGGGGGCTTTATACAGGTGTAGGATTAGGGTTCTAGACACGTATACAA

                                              CTG
                                               |
1. IL-1ra be 770       780       790       800|  810
[  594 ]    TGGCCTCAGAAGCAGGAGAGCTGGGTGGTATAAGGTCCTCTCAAGCTGGT>
            || || | |||  | |   |   |  |  | |  || |  |  || |
SEQ02_nuc   TGTCCCCCGAAATATGTCCACATCCTAATCCCAAGATCTGTGCATATGTT

                660       670       680       690       700
SEQ02_nuc   ACCATACATGTCCAAAGAGGTTTTGCAAATGTGATTATGTTAAGGATCTT
            TGGTATGTACAGGTTTCTCCAAAACGTTTACACTAATACAATTCCTAGAA

1. IL-1ra 820       830       840       850       860
[  594 ]    GCTGTGTA-GGCCACAAGGCATCTGC--ATGAG-TGACTTTAA-GA-C-T>
             |  |  | | |||  |  |  | |||  ||| | | |  |||| || | |
SEQ02_nuc   ACCATACATGTCCAAAGAGGTTTTGCAAATGTGATTATGTTAAGGATCTT
```

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                710        720        730        740        750
SEQ02_nuc       GAAATGAGGAGACAATCCTGGGTTATCCTTGTGGGCTCAGTTTAATCACA
                CTTTACTCCTCTGTTAGGACCCAATAGGAACACCCGAGTCAAATTAGTGT

1. IL-1ra be       870        880        890        900
[  594 ]        CAAA-GACCAAACACT-GAGCTTTCTTCTAG-GGG-TGGGTATGAAGATG>
                 ||| ||   | ||| |   |  || | || | ||| |  || | |   |
SEQ02_nuc       GAAATGAGGAGACAATCCTGGGTTATCCTTGTGGGCTCAGTTTAATCACA


                760        770        780        790        800
SEQ02_nuc       AGAAGGAGGCAGGAAGGGAGAGTCAGAGAGAGAATGGAAGATACCATGCT
                TCTTCCTCCGTCCTTCCCTCTCAGTCTCTCTCTTACCTTCTATGGTACGA

                     C                          ACTA
                     |                          |
1. IL-1ra b910       |920        930        940  |950
[  594 ]        CTTCAGAGTCATG-CGCGTTACCCA-CGATGGCATGGCACAGAGC-TG-A>
                     ||| || |  | |  |  ||  ||  | |||| | | | | ||
SEQ02_nuc       AGAAGGAGGCAGGAAGGGAGAGTCAGAGAGAGAATGGAAGATACCATGCT


                810        820        830        840        850
SEQ02_nuc       TCTAATTTTGAAGATGGAGTGAGGGGCCTTGAGCCAACAAATGCAGGTGT
                AGATTAAAAGTTCTACCTCACTCCCCGGAACTCGGTTTGTTTACGTCCACA

1. IL-1ra 960      970        980        990       1000
[  594 ]        TCTCTGTTTCTGTTTTGCTTTA-TTCCCTCTTGGGATGATATCATCCAGT>
                |||  |||     | |  | |    |||   |  |  | ||       ||
SEQ02_nuc       TCTAATTTTGAAGATGGAGTGAGGGGCCTTGAGCCAACAAATGCAGGTGT


                860        870        880        890        900
SEQ02_nuc       TTTTAGAAGGTGGAAAAGCCAAGGGAACGGATTCTCCTCTAGAGTCTCCG
                AAAATCTTCCACCTTTTCGGTTCCCTTGCCTAAGAGCAGATCTCAGAGGC

1. IL-1ra 1010     1020       1030       1040       1050
[  594 ]        CTTTA-TATGTTGCCAATATA-CCTCATTGTGTGT--AATAGAACCTTC->
                 |||| | || |  ||   |     |  |  | |    |||| || |
SEQ02_nuc       TTTTAGAAGGTGGAAAAGCCAAGGGAACGGATTCTCCTCTAGAGTCTCCG


                910        920        930        940        950
SEQ02_nuc       GAAGGAACACAGCTCTTGACACATGGATTTCAGCTCAGTGACACCCATTT
                CTTCCTTGTGTCGAGAACTGTGTACCTAAAGTCGAGTCACTGTGGGTAAA
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                              TAA          TTG
                               |            |
1. IL-1ra be    1060       1070   1080    1090      1100
[  594 ]     TTAGCATTA-AGACCTTGACAAAAATAATTCTGTTAAGTTAAATCATTTT>
               ||  |   | ||   |||||||  |    | ||| | | ||| | | |  |||
SEQ02_nuc    GAAGGAACACAGCTCTTGACACATGGATTTCAGCTCAGTGACACCCATTT


                    960       970       980       990       1000
SEQ02_nuc    CAGACTTCTGACCTCCACAACTATAAAATAATAAACTTGTGTTATTGTAA
             GTCTGAAGACTGGAGGTGTTGATATTTTATTATTTGAACACAATAACATT

                TAA                          A           G
                 |                           |           |
1. IL-1ra 1110  |1120       1130             |      1150 |    1160
[  594 ]     TGTCCTTGTAATGTGTA-ATCTTAAAGTTAATAAACTT-TGTTATT-TAT>
                 ||| | |   |  | | ||  ||  |||||||||| |||||| ||
SEQ02_nuc    CAGACTTCTGACCTCCACAACTATAAAATAATAAACTTGTGTTATTGTAA


                   1010      1020
SEQ02_nuc    ACCTCTAAAAAAAAAAAAAA
             TGGAGATTTTTTTTTTTTT

1. IL-1ra be        1170
[  594 ]     A-TAATAAAAAAAAAAAAAA>
             |    ||||||||||||||
SEQ02_nuc    ACCTCTAAAAAAAAAAAAAA
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EXHIBIT C

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                    10         20         30         40         50
SEQ02_nuc   CAGGGATCAGGGTTCCAGGAACTCAGGATCTGCAGTGAGGACCAGACACC
            GTCCCTAGTCCCAAGGTCCTTGAGTCCTAGACGTCACTCCTGGTCTGTGG

1. IL-1ra_nu  40          50          60          70          80
[  610 ]    GAGGCCTCCGCAG-TCACCTAATC--ACTC-TCCTCCTCTTCCT-GTTCC>
             |||  || |     ||   | ||    ||  |       ||     ||
SEQ02_nuc   CAGGGATCAGGGTTCCAGGAACTCAGGATCTGCAGTGAGGACCAGACACC


                    60         70         80         90         100
SEQ02_nuc   ACTGATTGCAGGAATGTGTTCCCTCCCCATGGCAAGATACTACATAATTA
            TGACTAACGTCCTTACACAAGGGAGGGGTACCGTTCTATGATGTATTAAT

1. IL-1ra_nu         90          100         110         120
[  610 ]    ATTCAGA-GAC-GATCT--GCCCACCCTCTG-GGAGAAAATCCAGCAAGA>
            | | |    |   || |   ||| |||  ||   ||| | | ||  | |
SEQ02_nuc   ACTGATTGCAGGAATGTGTTCCCTCCCCATGGCAAGATACTACATAATTA


                   110        120        130        140        150
SEQ02_nuc   AATATGCAGACCAGAAGGCTCTATACACAAGAGATGGCCAGCTGCTGGTG
            TTATACGTCTGGTCTTCCGAGATATGTGTTCTCTACCGGTCGACGACCAC

                        ATCT
                         |
1. IL-1ra_nu 130        140   150          160        170
[  610 ]    TGCAAG-CCTTCAGAGGGATG-TT-AACCAG-A-AGACCTTCTATCTGAG>
             | |     |||| || |   |  || ||   | ||  ||    | ||
SEQ02_nuc   AATATGCAGACCAGAAGGCTCTATACACAAGAGATGGCCAGCTGCTGGTG


                   160        170        180        190        200
SEQ02_nuc   GGAGATCCTGTTGCAGACAACTGCTGTGCAGAGAAGATCTGCACACTTCC
            CCTCTAGGACAACGTCTGTTGACGACACGTCTCTTCTAGACGTGTGAAGG

                    CAAC
                     |
1. IL-1ra_nu  180 | 190        200          210          220
[  610 ]    GAACAACTAGTTGCTGGATAC--TTGCAAGGACCAAATG-TC-AATTTAG>
            | | | |||| |   ||   ||   ||  | ||   |  |  | ||
SEQ02_nuc   GGAGATCCTGTTGCAGACAACTGCTGTGCAGAGAAGATCTGCACACTTCC
```

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                210        220        230        240        250
SEQ02_nuc   TAACAGAGGCTTGGACCGCACCAAGGTCCCCATTTTCCTGGGGATCCAGG
            ATTGTCTCCGAACCTGGCGTGGTTCCAGGGGTAAAAGGACCCCTAGGTCC

          AGAA                      GCCT
            |                         |
1. IL-1ra_nu|       240        250  |260        270        280
[  610 ]    AAAGATAGATGTGGTACCCATTGACATGCT-CTGTTCTTGGGAATCCATG>
            || | ||   |||   | ||   |  | |   | ||| |||| ||||| |
SEQ02_nuc   TAACAGAGGCTTGGACCGCACCAAGGTCCCCATTTTCCTGGGGATCCAGG


                260        270        280        290        300
SEQ02_nuc   GAGGGAGCCGCTGCCTGGCATGTGTGGAGACAGAAGAGGGGCCTTCCCTA
            CTCCCTCGGCGACGGACCGTACACACCTCTGTCTTCTCCCCGGAAGGGAT

1. IL-1ra_nu      290        300        310        320        330
[  610 ]    GAGGGAAGATGTGCCTGTCCTGTGTCAAGTCTGGTGATGAGACCAGACTC>
            ||||||      |||||| | |||||  || | |  || | | |    ||
SEQ02_nuc   GAGGGAGCCGCTGCCTGGCATGTGTGGAGACAGAAGAGGGGCCTTCCCTA


                310        320        330        340        350
SEQ02_nuc   CAGCTGGAGGATGTGAACATTGAGGAACTGTACAAAGGTGGTGAAGAGGC
            GTCGACCTCCTACACTTGTAACTCCTTGACATGTTTCCACCACTTCTCCG

1. IL-1ra_nu      340        350        360        370        390
[  610 ]    CAGCTGGAGGCAGTTAACATCACTGACCTGAGCGAGAACAGAAAGCAGGA>
            ||||||||||  || ||||     || ||  | |      |  |  |||
SEQ02_nuc   CAGCTGGAGGATGTGAACATTGAGGAACTGTACAAAGGTGGTGAAGAGGC


                360        370        380        390        400
SEQ02_nuc   CACACGCTTCACCTTCTTCCAGAGCAGCTCAGGCTCCGCCTTCAGGCTTG
            GTGTGCGAAGTGGAAGAAGGTCTCGTCGAGTCCGAGGCCGAAGTCCGAAC

                                    C
                                    |
1. IL-1ra_nu      390        400        410        420        430
[  610 ]    CAAGCGCTTCGCCTTCATC-CGCTCAACAGTGGCCCCACCACCAGTTTTG>
            ||  |||||| ||||| ||  |  || |    ||| || ||  |||  |||
SEQ02_nuc   CACACGCTTCACCTTCTTCCAGAGCAGCTCAGGCTCCGCCTTCAGGCTTG


                410        420        430        440        450
SEQ02_nuc   AGGCTGCTGCCTGGCCTGGCTGGTTCCTGTGTGGCCCGGCAGAGCCCCAG
            TCCGACGACGGACCGGACCGACCAAGGACACACCGGGCCGTCTCGGGGTC

1. IL-1ra_nu      440        450        460        470        480
[  610 ]    AGTCTGCCGCCTGCCCCGGTTGGTTCCTCTGCCACAGCGATGGAAGCTGAC>
            || |||| |||||  || ||  |||||||| ||     ||   ||  |  |
SEQ02_nuc   AGGCTGCTGCCTGGCCTGGCTGGTTCCTGTGTGGCCCGGCAGAGCCCCAG
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                460        470        480        490        500
SEQ02_nuc   CAGCCAGTACAGCTCACCAAGGAGAGTGAGCCCTCAGCCCGTACCAAGTT
            GTCGGTCATGTCGAGTGGTTCCTCTCACTCGGGAGTCGGGCATGGTTCAA

                      G                GACG
                      |                |
1. IL-1ra_nu      490 |    500         |    520        530
[  610 ]    CAGCCCG-TCACCTCACCAATATGCCTAAGGCGTC-ATGGTCACCAAATT>
            ||||| |  || |||||||||   |  | || | ||        ||||| ||
SEQ02_nuc   CAGCCAGTACAGCTCACCAAGGAGAGTGAGCCCTCAGCCCGTACCAAGTT


                510        520        530        540        550
SEQ02_nuc   TTACTTTGAACAGAGCTGGTAGGGAGACAGGAAACTGCGTTTTAGCCTTG
            AATGAAACTTGTCTCGACCATCCCTCTGTCCTTTGACGCAAAATCGGAAC

1. IL-1ra_nu  540        550        560        570        580
[  610 ]    CTACTTCCAGGAGGACGAGTAGTACTGCCCAGGCCTG-CTGT--TCCA-T>
             ||||| |  ||  |  ||||     |       |||  | |   ||
SEQ02_nuc   TTACTTTGAACAGAGCTGGTAGGGAGACAGGAAACTGCGTTTTAGCCTTG


                560        570        580        590        600
SEQ02_nuc   TGCCCCCAAACCAAGCTCATCCTGCTCAGGGTCTATGGTAGGCAGAATAA
            ACGGGGGTTTGGTTCGAGTAGGACGAGTCCCAGATACCATCCGTCTTATT

1. IL-1ra_nu      590
[  610 ]    -TCTTGCATGGCAA>
              |  ||  |||
SEQ02_nuc   TGCCCCCAAACCAA


                610        620        630        640        650
SEQ02_nuc   TGTCCCCCGAAATATGTCCACATCCTAATCCCAAGATCTGTGCATATGTT
            ACAGGGGGCTTTATACAGGTGTAGGATTAGGGTTCTAGACACGTATACAA


                660        670        680        690        700
SEQ02_nuc   ACCATACATGTCCAAAGAGGTTTTGCAAATGTGATTATGTTAAGGATCTT
            TGGTATGTACAGGTTTCTCCAAAACGTTTACACTAATACAATTCCTAGAA


                710        720        730        740        750
SEQ02_nuc   GAAATGAGGAGACAATCCTGGGTTATCCTTGTGGGCTCAGTTTAATCACA
            CTTTACTCCTCTGTTAGGACCCAATAGGAACACCCGAGTCAAATTAGTGT


                760        770        780        790        800
SEQ02_nuc   AGAAGGAGGCAGGAAGGGAGAGTCAGAGAGAGAAATGGAAGATACCATGCT
            TCTTCCTCCGTCCTTCCCTCTCAGTCTCTCTCTTACCTTCTATGGTACGA


                810        820        830        840        850
SEQ02_nuc   TCTAATTTTGAAGATGGAGTGAGGGGCCTTGAGCCAACAAATGCAGGTGT
            AGATTAAAACTTCTACCTCACTCCCCGGAACTCGGTTGTTTACGTCCACA
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                860        870        880        890        900
SEQ02_nuc   TTTAGAAGGTGGAAAAGCCAAGGGAACGGATTCTCCTCTAGAGTCTCCG
            AAAATCTTCCACCTTTTCGGTTCCCTTGCCTAAGAGGAGATCTCAGAGGC

                910        920        930        940        950
SEQ02_nuc   GAAGGAACACAGCTCTTGACACATGGATTTCAGCTCAGTGACACCCATTT
            CTTCCTTGTGTCGAGAACTGTGTACCTAAAGTCGAGTCACTGTGGGTAAA

                960        970        980        990       1000
SEQ02_nuc   CAGACTTCTGACCTCCACAACTATAAAATAATAAACTTGTGTTATTGTAA
            GTCTGAAGACTGGAGGTGTTGATATTTTATTATTTGAACACAATAACATT

               1010       1020
SEQ02_nuc   ACCTCTAAAAAAAAAAAAAA
            TGGAGATTTTTTTTTTTTTT
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